Trial record **1 of 1** for: GS-US-401-2076

Previous Study | Return to List | Next Study

Safety and Efficacy of the Combination of Tirabrutinib and Entospletinib With and Without Obinutuzumab in Adults With Chronic Lymphocytic Leukemia (CLL)

This study is currently recruiting participants.

See Contacts and Locations

Verified October 2017 by Gilead Sciences

Sponsor:
Gilead Sciences

ClinicalTrials.gov Identifier:
NCT02983617

First Posted: December 6, 2016
Last Update Posted: October 13, 2017

Collaborator:
German CLL Study Group

Information provided by (Responsible Party):
Gilead Sciences

Full Text View | Tabular View | No Study Results Posted | Disclaimer
How to Read a Study Record

Purpose

The primary objective of this study is to determine the preliminary efficacy of the combination of tirabrutinib (formerly GS-4059) and entospletinib with obinutuzumab in adults with relapsed or refractory chronic lymphocytic leukemia (CLL).

The secondary objective is evaluation of safety and evaluation of additional parameters of efficacy. The treatment period is adaptive, with a duration of active treatment up to two years and a total follow-up on study of 5 years for time-dependent outcome variables. The study has a 6 patient per arm safety run-in to evaluate safety prior to the enrollment of subsequent participants.

Condition	Intervention	Phase
Chronic Lymphocytic Leukemia	Drug: Tirabrutinib Drug: Entospletinib Drug: Obinutuzumab	Phase 2

Study Type: Interventional

Study Design: Allocation: Non-Randomized
Intervention Model: Parallel Assignment
Masking: None (Open Label)
Primary Purpose: Treatment

Official Title: A Prospective, Randomized, Open-Label, Multicenter, Phase 2 Trial to Evaluate the Safety and Efficacy of the Combination of Tirabrutinib (GS-4059) and Entospletinib With and Without Obinutuzumab in Subjects With Chronic Lymphocytic Leukemia

Resource links provided by NLM:

MedlinePlus related topics: Chronic Lymphocytic Leukemia Leukemia

Drug Information available for: Obinutuzumab

Genetic and Rare Diseases Information Center resources: Chronic Lymphocytic Leukemia Leukemia, B-cell, Chronic

U.S. FDA Resources

Further study details as provided by Gilead Sciences:

Primary Outcome Measures:

- Rate of Complete Remission (CR) as Assessed by the Investigator Using the Modified International Workshop on CLL (IWCLL) 2008 criteria [Time Frame: After the completion of 24 weeks of treatment]

Secondary Outcome Measures:

- Rate of CR with Bone Marrow Minimal Residual Disease (MRD) Negativity [Time Frame: After the completion of 24 weeks of treatment]
- Rate of CR with Peripheral Blood MRD Negativity [Time Frame: After the completion of 24 weeks of treatment]
- Overall Response Rate (ORR) [Time Frame: After the completion of 24 weeks of treatment]
- Duration of Response (DOR) [Time Frame: After the completion of 24 weeks of treatment]
- Progression-Free Survival [Time Frame: Up to 5 years]
- Overall Safety as Assessed by the Frequency of Treatment-Emergent Adverse Events (AE) and Treatment-Emergent Serious AEs [Time Frame: Up to 5 years]

Estimated Enrollment:	36
Actual Study Start Date:	April 6, 2017
Estimated Study Completion Date:	November 2022
Estimated Primary Completion Date:	December 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Tirabrutinib + entospletinib Participants will receive tirabrutinib and entospletinib for up to 104 weeks.	Drug: Tirabrutinib 80 mg (1 x 80 mg or 4 x 20 mg) tablets administered orally once daily Other Name: GS-4059 Drug: Entospletinib 400 mg (2 x 200 mg) tablets administered orally once daily Other Name: GS-9973
Experimental: Tirabrutinib + entospletinib + obinutuzumab Participants will receive obinutuzumab over 21 weeks and the combination of tirabrutinib and entospletinib for up to 104 weeks.	Drug: Tirabrutinib 80 mg (1 x 80 mg or 4 x 20 mg) tablets administered orally once daily Other Name: GS-4059 Drug: Entospletinib

	400 mg (2 x 200 mg) tablets administered orally once daily Other Name: GS-9973 Drug: Obinutuzumab 1000 mg/40 mL single-use vials administered intravenously for a total of 8 doses over 21 weeks Other Names: • Gazyvaro® • Gazyva® • GA101

Eligibility

Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Senior)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Key Inclusion Criteria:

- Documentation of relapsed or refractory CLL
- Requiring treatment per modified IWCLL 2008 criteria; adults without radiographically measureable disease (defined as ≥ 1 lesion > 1.5 cm in diameter as assessed by computed tomography (CT) or magnetic resonance imaging (MRI)) must have bone marrow evaluation at screening
- Adequate hematologic function: platelet count ≥ 50 × 10^9/L, neutrophil count ≥ 1 × 10^9/L, hemoglobin ≥ 8 g/dL unless lower values are directly attributable to documented bone marrow burden of CLL

- Creatinine clearance (CrCl) ≥ 50 mL/min
- Total bilirubin ≤ 1.5× institutional upper limit of normal (ULN) unless attributed to Gilbert's syndrome and aspartate transaminase (AST)/alanine transaminase (ALT) ≤ 2.5×ULN
- Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) ≤ 2
- Absence of active HIV, hepatitis B virus (HBV) infection, and hepatitis C virus (HCV) infection
- Satisfies the following criteria:
    - For females of childbearing potential, willingness to abstain from sexual intercourse or use a protocol-specified method of contraception as described in the study protocol
    - Males of reproductive potential who engage in sexual intercourse must agree to use protocol-specified method(s) of contraception as described in the study protocol
- Able to comply with study procedures and restrictions

Key Exclusion Criteria:

- Known transformation of CLL (ie, Richter's transformation, prolymphocytic leukemia)
- Known central nervous system (CNS) involvement
- Progression on treatment with any inhibitor of Bruton's tyrosine kinase (BTK), spleen tyrosine kinase (SYK), phosphatidylinositol 3-kinase (PI3K), B-cell lymphoma 2 (BCL-2), or obinutuzumab. The treatment and disease response history of participants with prior treatment with agents in these classes should be reviewed by the sponsor or the German CLL Study Group office prior to enrollment to clarify sensitivity to these treatments
- Any treatment for CLL other than corticosteroids for symptomatic management within 28 days of the start of study treatment
- Participation on a concurrent therapeutic clinical trial unless all treatment is complete with only ongoing surveillance
- Diagnosis of or concern for progressive multifocal leukoencephalopathy
- History of myelodysplastic syndrome or another malignancy other than CLL, except for the following: any malignancy that has been in complete remission for 3 years, adequately treated local basal cell or squamous cell carcinoma of the skin, cervical carcinoma in situ, superficial bladder cancer, asymptomatic prostate cancer without known metastatic disease and with no requirement for therapy or requiring only hormonal therapy and with normal prostate-specific antigen for ≥1 year prior to start of study therapy
- Active infection requiring systemic therapy
- Pregnant or nursing women (a negative pregnancy test is required for all women of childbearing potential within 7 days before start of treatment and monthly during therapy)
- Active autoimmune disease or the need for higher than prednisone 10 mg daily unless for management of CLL symptoms

- History of stroke or intracranial hemorrhage within 12 months of randomization; subjects requiring therapeutic anticoagulation for any indication should be discussed with the German CLL Study Group (GCLLSG) cooperating physician and/or medical monitor prior to screening.
- Anticipated chronic use of strong CYP3A4/CYP2C9 inducers, moderate CYP2C9 inducers, or strong P-gp inducers while on study; use within 2 weeks of first dose of study treatment should be avoided.
- Requirement for proton pump inhibitor (PPI) therapy
- Demonstration of corrected QT (QTc) interval > 450 milliseconds or requirement for ongoing treatment with concomitant medications that prolong the QT interval

Note: Other protocol defined Inclusion/Exclusion criteria may apply.

Contacts and Locations

Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT02983617***

Contacts

Contact: Gilead Study Team 1-833-GILEAD-0(1-833-445-3230) **GS-US-401-2076**@gilead.cor

Locations

Germany

Kreiskliniken Reutlingen GmbH Klinikum am Steinenberg
Reutlingen, Baden-wuerttemberg, Germany

Universitätsklinikum Essen Klinik für Hämatologie
Essen, Nordrhein-westfalen, Germany

Uniklinik Köln Klinik I für Innere Medizin
Köln, Nordrhein-westfalen, Germany

Praxis für Hämatologie und Onkologie

Saarbrücken, Saarland, Germany

Gesundheitszentrum St. Marien GmbH
Amberg, Germany, 92224

Studienzentrum Aschaffenburg
Aschaffenburg, Germany

Evangelisches Diakoniekrankenhaus Bremen Hämatologie
Bremen, Germany

St.-Johannes-Hospital
Dortmund, Germany

University Medical Center Freiburg
Freiburg, Germany

OncoResearch Lerchenfeld GmbH
Hamburg, Germany

Universitätsklinikum Heidelberg, Abteilung Innere Medizin V
Heidelberg, Germany

Westpfalz-Klinikum GmbH
Kaiserslautern, Germany

Universitätsklinikum Schleswig-Holstein Klinik für Innere Medizin II - Hämatologie und Onkol
Kiel, Germany

Klinikum Lippe Lemgo
Lemgo, Germany

Mannheimer Onkologie Praxis
Manheim, Germany, 68161

Städtisches Klinikum München GmbH Klinikum Schwabing
München, Germany

Gemeinschaftspraxis für Hämatologie und Onkologie
Münster, Germany

Robert-Bosch-Krakenhaus
Stuttgart, Germany

Universitätsklinik Ulm - Klinik für Innere Medizin III
Ulm, Germany

Sozialstiftung Bamberg
Würzburg, Germany, 97080

Universitatsklinikum Wurzburg
Würzburg, Germany

Sponsors and Collaborators

Gilead Sciences

German CLL Study Group

Investigators

Study Director: Gilead Study Director Gilead Sciences

More Information

Responsible Party:	Gilead Sciences
ClinicalTrials.gov Identifier:	NCT02983617 History of Changes
Other Study ID Numbers:	**GS-US-401-2076**
	2016-002768-15 (EudraCT Number)
	CLLRUmbrella2 (Other Identifier: German CLL Study Group)
First Submitted:	December 2, 2016
First Posted:	December 6, 2016
Last Update Posted:	October 13, 2017
Last Verified:	October 2017

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Product Manufactured in and Exported from the U.S.:	Yes

Additional relevant MeSH terms:

Leukemia	Lymphatic Diseases
Leukemia, Lymphoid	Immunoproliferative Disorders
Leukemia, Lymphocytic, Chronic, B-Cell	Immune System Diseases
Neoplasms by Histologic Type	Leukemia, B-Cell
Neoplasms	Obinutuzumab
Lymphoproliferative Disorders	Antineoplastic Agents